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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,177	03/29/2004	Wei Gu	5199-178	5834

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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

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10/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/813,177	**Applicant(s)** GU ET AL.	
	Examiner Brandon J. Fetterolf, PhD	**Art Unit** 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 31 August 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *47,48,54,57 and 61-63*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☒ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). 1/7/2005
13. ☐ Other: _____.

DETAILED ACTION

Response to the Amendment

The Amendment filed on 8/31/2007 in response to the previous Final Office Action (5/31/2007) is acknowledged, but has not been entered. The amendment has not been entered because it contains claim limitations, which were not previously searched and/or considered. For example, Claim 54 is drawn to a method for determining whether an agent is reactive with Mdm2 comprising the steps of contacting a candidate agent with Mdm2, in the presence of herpesvirus-associated ubiquitin-specific protease (HASUP); and (b) determining whether the candidate agent inhibits Mdm2-HAUSP protein complex formation, wherein inhibition of Mdm2-HAUSP protein complex formation indicates that the agent is reactive with Mdm2. Similarly, Claim 57 recites a method for determining whether an agent is reactive with HAUSP comprising the steps of contacting a candidate agent with HAUSP, in the presence of Mdm2; and (b) determining whether the candidate agent inhibits Mdm2-HAUSP protein complex formation, wherein inhibition of Mdm2-HAUSP protein complex formation indicates that the agent is reactive with HAUSP. Thus, the claims appear to encompass determining the same Mdm2-HAUSP protein complex for the determination of an active agent against two distinct proteins; and therefore, would require further consideration with respect to 112, 2nd paragraph, as well as 112, 1st paragraph enablement.

Claims 47-48, 54, 57, 61-63 are currently pending and under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed 1/7/2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Response to Arguments

As Applicant's arguments appear to be solely drawn to the current Amendment file on 8/31/2007, which has not been entered, such arguments have not been considered.

As such the following rejections are maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47-48, 54, 57 and 61-63 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 47, 54 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the active of steps of determining. In the instant case, it is unclear what activity is being determined or how this activity and/or interaction is being determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 61 remains rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 61 recites a method for determining whether an agent affects one or more Mdm2-associated, HAUSP-associated, or p53 associated biological events in a cell, comprising the steps of contacting a cell with an agent that is reactive with Mdm2 or HAUSP, as determined by the method of claim 54 or 57. Thus, the claims encompass using a genus of molecules identified in a screening assay.

The specification teaches that modulators of MDM2 and HAUSP can be easily identified by simple screening assays. For example, the specification teaches that cells (e.g., MDM2-null cells or cells comprising MDM2) can be plated onto microtiter plates, then contacted with a library of drugs (paragraph 00128). In particular, the specification teaches that modulators include, but are not limited to, proteins, polypeptides, peptides, nucleic acids (including DNA or RNA), antibodies and fragments thereof, molecules, compounds, antibiotics, drugs, an agent reactive with HAUSP that induces or upregulates HAUSP expression, an agent reactive with MDM2 that induces or

upregulates MDM2 expression, and an agent reactive with an MDM2-HAUSP complex. Thus, while the specification contemplates a number of potential modulators which can be used a screening assay, the written description does not appear to be commensurate in scope with the claimed invention because the claims encompass a genus of compounds defined only by their function wherein the relationship between the structural features of members of the genus and said function have not been defined. In the absence of such a relationship either disclosed in the as filed application or which would have been recognized based upon information readily available to one skilled in the art, the skilled artisan would not know how to make and use compounds that lack structural definition. The fact that one could have assayed a compound of interest using the claimed assays does not overcome this defect since one would have no knowledge beforehand as to whether or not any given compound (other than those that might be particularly disclosed in an application) would fall within the scope of what is claimed. It would require undue experimentation (be an undue burden) to randomly screen undefined compounds for the claimed activity.

Although the description does not provide working examples, the description teaches a method for measuring the biochemical and binding activity of the specific MDM2-HAUSP interaction, and the person skilled in the art can understand how to use the screening method considering the common general knowledge.

To comply with the written description requirement of 35 U.S.C. § 112, first paragraph, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention Edith all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was Already for patenting" such as by the use of drawings or structural chemical formulas that show that the invention was complete, or describing distinguishing identifying characteristics sufficient to show that the applicant was in Possession of the claimed invention.

Claimed invention is drawn to an agent identified by the method of claims 54 or 57. However, no structural or specific functional characteristics of such an agent is provided, nor is there any indication that the artisan actually implemented the method of claims 54 or 57 so as to

identify any agent. This situation is analogous to that of *Regents of the University of California v Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). Because one skilled in the art would conclude that the inventors were not in possession of the claimed invention. The claim fails to comply with the written description requirement.

Therefore, No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

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